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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/739,933	12/18/2000	James Steven Reid	E8019-00001	4882

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EXAMINER	
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ART UNIT	PAPER NUMBER
1649	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/739,933	REID ET AL.	
	Examiner	Art Unit	
	STACEY MACFARLANE	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 December 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,5-8,33,63-66 and 70-72* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,5-8,33,63-66 and 70-72* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/02/2010*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Response to Amendment

1. Claim 73 has been cancelled. Claims 1, 2, 5, 33, 63, 65, 66 and 70-72 have been amended, as requested in the amendment filed on December 2, 2010. Following the amendment, claims 1, 2, 5-8, 33, 63-66 and 70-72 are pending in the instant application and are under examination in the instant office action.

Priority

2. In view of current claim amendments to remove the sequence $CX_7CX_4CX_{10}CXCX_8C$ (SEQ ID NO: 1) from the claims, Applicant's claim for the benefit of a prior-filed application under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is acknowledged. Pending claims 1, 2, 5-8, 33, 63-66 and 70-72 will be given the benefit of the filing date of the provisional application, August 4, 1997.

Claim Objections (New, Necessitated by Amendment)

3. As currently amended, Claim 33 is objected to under 37 CFR 1.75 as being a substantial duplicate of claim 1. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

4. Claim 70 is objected to for improper punctuation. There are two periods at the end of the claim. Appropriate correction is required.

Claim Rejections - 35 USC § 112 (New, Necessitated by Amendment)

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 2 and 8 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

7. Claim 2 is missing active method steps leading to the stimulation of differentiation of the neural progenitor cell. Absent such steps the claim appears to merely encompass a result of the administration step and fail to distinguish from the subject matter of the parent claim.

8. Claim 8 is indefinite in that it recites "spinal nerve root origins" which a skilled artisan would recognize as the dorsal or ventral roots of the spinal cord. Claim 8, however, the claim depends from claim 1 which recites a Markush group of tissues, none of which are within the spinal cord. Therefore there is, at the very least, a lack of antecedent basis for the term "spinal nerve root origins" within the parent claim.

Claim Rejections - 35 USC § 102 (New, Necessitated by Amendment)

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

As currently amended, Claims 1, 5-7, 33, 63-65 and 70 are rejected under 35 U.S.C. 102(b) as being anticipated by Loughlin et al. (1992) cited on the IDS mailed 8/28/2008.

Claims 1, 5-7, 33, 63-65 and 70 are drawn to a method comprising the sole active step of administering to a subject having CNS damage or lesion a therapeutically effective amount of a composition comprising TGF-alpha wherein said administration is outside of the ventricles and wherein the effects are evidenced by an amelioration of behavioral deficits attributable to the damage or lesion (claim 70); wherein the location is selected from striatum, pallidum, septum, cortex, external capsule, internal capsule, substantia nigra-ventral tegmentum, and at or adjacent to an ependymal or subependymal zone (claims 1, 33 and 65); wherein the composition is administered by intrastriatal infusion (claims 5, 63 and 64); to a CNS brain tissue adjacent to the SEZ (claim 7); administration is for a period of at least sixteen days (claim 65).

It should be noted that there is no explicit definition for the “subject” of the claims. The Loughlin et al. prior art teaches a method comprising administering TGF-alpha by intrastriatal infusion for "over a two week period" to animals that have a 6-OHDA lesion. It is well-recognized within the art that the striatum is adjacent to the SEZ, as required by instant claim 7. The Loughlin et al. art further teaches rotation behavior was analyzed for effect of treatment, with those animals having TGF-alpha infusion exhibiting significantly decreased rotation behavior.

The Loughlin et al. prior art is silent with respect to “attracting neural progenitor cells” or “effect[ing] migration of the neural progenitor cell”, yet the Loughlin et al. art

recites the active step required by the method. Thus, absent additional method steps to distinguish over the art, the method inherently leads effects migration or attracts neural progenitor cells. MPEP § 2112 provides guidance as to the Examiner's burden of proof for a rejection of claims under 35 U.S.C. 102 or 103 based upon the express, implicit, and inherent disclosures of a prior art reference. The case law clearly states that something which is old does not become patentable upon the discovery of a new property. *Atlas Powder Co. v. Ireco Inc.*, 190 F.3d 1342, 1347, 51 USPQ2d 1943, 1947 (Fed. Cir. 1999); *In re Best*, 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977). Further, the court has held that there is no requirement that a person of ordinary skill in the art would have recognized the inherent disclosure at the time of invention, but only that the subject matter is in fact inherent in the prior art reference. *Schering Corp. v. Geneva Pharm. Inc.*, 339 F.3d 1373, 1377, 67 USPQ2d 1664, 1668 (Fed. Cir. 2003); see also *Toro Co. v. Deere & Co.*, 355 F.3d 1313, 1320, 69 USPQ2d 1584, 1590 (Fed. Cir. 2004) ("[T]he fact that a characteristic is a necessary feature or result of a prior-art embodiment (that is itself sufficiently described and enabled) is enough for inherent anticipation, even if that fact was unknown at the time of the prior invention."); *Abbott Labs v. Geneva Pharms., Inc.*, 182 F.3d 1315, 1319, 51 USPQ2d 1307, 1310 (Fed.Cir.1999).

The case law specifically applies to the instant application where Applicant has claimed a method in terms of a functional effect and the method of the prior art is materially and methodologically the same as that of the claim, but the function is not explicitly disclosed by the reference. The examiner's assertion of inherency is based

upon the structural similarity between the patented composition and the claimed composition.

Where the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a *prima facie* case of either anticipation or obviousness has been established and the burden of proof rests upon the Applicant to demonstrate that the prior art does not necessarily or inherently possess the characteristics of Applicant's claimed product. *In re Fitzgerald*, 619 F.2d 67, 70, 205 USPQ 594, 596 (CCPA 1980) (quoting *In re Best*, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977)). "When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not." *In re Spada*, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990).

Claim Rejections - 35 USC § 103 (New, Necessitated by Amendment)

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

11. Claims 1, 2, 5-8, 33, 63-66 and 70-72 stand as rejected under 35 U.S.C. 103(a) as being unpatentable over Loughlin et al. (1992) as applied to claims 1, 5-7, 33, 63-65 and 70 above and further in view of Weiss et al. US Patent 5,980,885, filed June 7, 1995, cited in Office action mailed 8/5/2002.

On pages 14-15 of Remarks filed December 2, 2010, Applicant traverse the rejection on the grounds that the amended claims represent non-obvious selection that is characterized by unexpected and surprising results over the prior art. Specifically, the claims have been amended to recite three inventive selections, namely, (1) the use of TGF-alpha to treat neurological injuries; (2) administration outside the ventricles; and (3) the combination of TGF-alpha and extra-ventricular administration. Applicant argues that the Weiss prior art "places no particular emphasis on TGF-alpha" (Remarks, page 15) and Weiss does not provide experiments in support of specific effects of TGF-alpha on neurosphere production (*Id*, page 16, referring to Table II of Weiss). Applicant concludes that within the prior art there are "no blazemarks pointing to TGF-alpha or suggesting it has any special properties or effects in cell proliferation, neurogenesis and the resulting amelioration of behavioral effects" (*Id*, page 16).

While this has been considered in full it is not found persuasive for the following reasons. The Loughlin et al. prior art explicitly teaches that it was known in the prior art that administration of TGF-alpha by intrastriatal infusion for a two week period provided therapeutic treatment to subjects having a CNS lesion, and that efficacy could be assessed by behavioral effects.

Firstly, as every Patent is valid the Weiss et al. is enabled for methods comprising TGF-α. Even though there may be no specific working example for its administration, the use of other the growth factors in the disclosed methods for promoting proliferation of neural stem cell progeny disclosed by Weiss, would not constitute undue further experimentation. Furthermore, the Weiss Patent explicitly

contemplates use of the method at the site of damage or lesion where promotion of proliferation and differentiation of neural stem cell progeny would effect treatment of neurological injuries or disease. Additionally, the Weiss Patent teaches that the invention provides a means for generating large numbers of undifferentiated and differentiated neural cells in vivo, arising from the ependymal zone, as required by instant claim 72 (Column 13 lines 21-41).

The Declaration by named inventor Dr. James Fallon filed on December 2, 2010 under 37 CFR 1.132 has been considered but is ineffective to overcome the rejection based upon prior art. While the second set of experiments described within the declaration demonstrate the link between TGF-alpha and cell proliferation, the materials and method steps are identical to those described within the Loughlin et al. prior art. Again, the discovery of a new functional effect or property of a known method does not provide a preponderance of evidence in support of unexpected results.

In assessing the weight to be given expert testimony, the examiner may properly consider, among other things, the nature of the fact sought to be established, the strength of any opposing evidence, the interest of the expert in the outcome of the case, and the presence or absence of factual support for the expert's opinion. See Ex parte Simpson, 61 USPQ2d 1009 (BPAI 2001), Cf. Redac Int'l. Ltd. v. Lotus Development Corp., 81 F.3d 1576, 38 USPQ2d 1665 (Fed. Cir. 1996), Paragon Podiatry Lab., Inc. v. KLM Lab., Inc., 948 F.2d 1182, 25 USPQ2d 1561, (Fed. Cir. 1993). Affidavits or declarations are provided as evidence and must set forth facts, not merely conclusions. In re Pike and Morris, 84 USPQ 235 (CCPA 1949).

Dr. Fallon is one of the two named inventors and, therefore, has a vested interest in the outcome of the case. The experimental evidence presented in the declaration is provided as evidence of unexpected results over those experiments described within

the prior art. The declaration describes two sets of experiments: (1) the intracerebroventricular administration of growth factors to a Parkinson's disease animal model (the 6-OHDA lesion model) versus control which lead to "no significant or useful cell proliferation or migration ... and had no effect on behavioral or functional recovery" (bullet 13); and (2) experiments that intrastriatal administration of TGF-alpha leads to a sustained proliferative and migratory effect of cells. As stated above, the experiments described are identical to those described by the Loughlin et al. prior art, which explicitly decribes behavioral effects. Therefore, the preponderance of evidence presented, in view of the current art applied, is not persuasive to demonstrate unexpected results over the prior art.

Examiner maintains that the elements of the methodology were disclosed in the Loughlin et al. prior art and the behavioral effects of TGF-alpha administration are disclosed. Examiner provides further evidence that it was known in the art at the time of filing that TGF-alpha affects neural progenitor cell proliferation and migration (Weiss et al. Patent). Thus, given the teachings within the art, there is insufficient evidence in support of unexpected results, and the invention as a whole is prima facie obvious in view of the art at the time of filing.

Double Patenting

12. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct

from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

13. Claims 1, 5, 6, 33, 63, 65 and 70-72 stand as provisionally rejected on the grounds of provisional nonstatutory obviousness-type double patenting as being unpatentable over claims 45, 48, 55 and 57-60 of copending Application No. 09/129,028.

14. Applicant has not traversed this rejection but has requested that it be held in abeyance until allowable subject matter is identified.

15. Claims 1, 5, 6, 33, 63, 65 and 70-72 are provisionally rejected on the ground of provisional nonstatutory obviousness-type double patenting as being unpatentable over claims 1-3, 12-13, 41, 43, 53, 54 and 61-65 of copending Application No. 10/167,384.

16. Applicant has not traversed this rejection but has requested that it be held in abeyance until allowable subject matter is identified.

17. Applicants are advised that traversal of the above rejections at a later date, presuming the claims stand substantively as they are now, will not be considered to be timely.

Conclusion

18. No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to STACEY MACFARLANE whose telephone number is (571)270-3057. The examiner can normally be reached on M-R 5:45 to 3:30, TELEWORK-Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Stucker can be reached on (571) 272-0911. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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